

REMARKS

Applicant acknowledges receipt of an Advisory Action dated December 23, 2008. In this response, Applicant has amended claims 22 and 28. Support for this amendment can be found, for example, at page 8, line 14 – page 9, line 5 of the originally filed specification. Claims 22-41 remain pending in the application.

This response supplements the prior response submitted on August 13, 2008, and responds to both the Final Office Action of May 13, 2008 and the Advisory Action of December 23, 2008.

Applicant respectfully requests reconsideration of the present application in view of the reasons that follow.

Response to Advisory Action of December 23, 2008

In the Advisory Action of December 23, 2008 the Office states:

[a]dditionally, Examiner advises Applicants [sic] to take notice of the language used in method claims 22 and 28, which do not necessitate an interpretation that involves a physical transformation or one that involves a corresponding defined structure. Therefore, Examiner need not assume that Applicants [sic] are claiming the structure that they seem to be arguing such as a ‘photodetector’ or ‘radiodetector’ or the simultaneous use of the former and latter as suggested in (page 8, last paragraphs, Arguments filed 8/13/2008).

Applicant respectfully disagrees. To advance prosecution, claims 22 and 28 have been amended as discussed above. Applicant further submits that the primary reference of Rabito does not disclose all features of the independent claims. For example:

I. Rabito fails to teach: “...simultaneously determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers at identical projection angles...” (emphasis added).

On page 2 of the Advisory Action of December 23, 2008, the Office states that “...Rabito teaches detecting fluorescence substances and detecting radioactive substances (col. 15, lines 50-56).” Applicant submits that the Office has not actually established that

Rabito teaches simultaneous determination of both bioluminescent and/or fluorescent markers, and radioactive markers.

For example, on page 2 of the Office Action of May 13, 2008, the Office states:

[f]urthermore, Rabito teaches that two or more markers with different emission energies can be used simultaneously (col. 15, lines 42-50). Furthermore, Rabito teach that one marker can be used for GFR and another marker can be used for perfusion measurements (col. 15, lines 50-55). This would then include using one fluorescent marker and one radioactive marker, especially since Rabito's specification teaches numerous instances of using both fluorescent and radioactive markers to measure renal function.

The Office attempts to supplement this argument by adding that "Rabito does ALSO teach the use of the simultaneous detection of markers with different radiation energies (which would include fluorescent radiation)". See Advisory Action at page 2.

The Office, however, has not established that the labeled substances of Rabito, that is the labeled substance effective for determining GFR and the labeled substance for determining kidney perfusion rate, ultimately provide both fluorescent and radioactive emission energies to support the premise that Rabito provides a method of detecting both energies simultaneously.

In other words, Applicant submits that the Rabito fails to teach that detection of GFR labels and perfusion measurement labels would require "...simultaneously determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers..." as recited in claim 22.

II. Rabito also fails to teach "... separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector...and...simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector" (Emphasis added).

On page 2 of the Advisory Action of December 23, 2008, the Office states that "...Rabito teaches detecting fluorescence substances and detecting radioactive substances (col. 3, 53-64)". Applicant submits the Office has impermissibly mixed and matched terms,

phrases and concepts found in Rabito to form a basis for rejecting independent claim 22 which is ultimately improper.

For example, while Rabito mentions the concepts of detection of fluorescent substances, the detection of radioactive substances, as well as the terms “radiodetector” and “photodetector”, Rabito does not disclose a single instance in which all of these are used together as part of a single method.

Contrary to the Office’s misinterpretation of Rabito, the reference, at col. 3 lines 55-58, explicitly states the following: “In some preferred embodiments the detectable substance is radioactive, and the detector includes a radiodetector; OR, the detectable substance is fluorescent, and the detector includes a photodetector...” (emphasis added). Applicant submits that it is apparent in col. 3, lines 55-58, that Rabito apparatus and method seeks to include only one type of detector for measuring one type of substance that emits one type of energy.

III. Rabito fails to teach: “...alternately determining in vivo distributions of bioluminescent and/or fluorescent markers and in vivo distributions of radioactive markers with a common measurement apparatus at identical projection angles...” (Emphasis added).

On page 2 of the Advisory Action of December 23, 2008, the Office states that “...Rabito teaches detecting fluorescence substances and detecting radioactive substances (col. 15, lines 50-56).” Applicant submits that the Office has not established that Rabito actually teaches alternately determining in vivo distribution of fluorescent markers and radioactive markers in a single method.

For example, on page 2 of the Office Action of May 13, 2008, the Office states:

[f]urthermore, Rabito teaches that two or more markers with different emission energies can be used simultaneously (col. 15, lines 42-50). Furthermore, Rabito teach that one marker can be used for GFR and another marker can be used for perfusion measurements (col. 15, lines 50-55). This would then include using one fluorescent marker and one radioactive marker, especially since Rabito’s specification teaches numerous instances of using both fluorescent and radioactive markers to measure renal function.

The Office attempts to supplement this argument in the Advisory Action by adding that “Rabito does ALSO teach the use of the simultaneous detection of markers with different radiation energies (which would include fluorescent radiation)”. Applicant points out that in the Advisory Action, the Office attempts to only emphasize Rabito with respect to a teaching of the simultaneous measurement feature of claim 22, and does not address the “alternately determining” feature of claim 28 at all.

Furthermore the Office’s has not established that the labeled substance effective for determining GFR and the labeled substance for determining kidney perfusion rate, as discussed in Rabito, ultimately provide fluorescent and radioactive emission energies. In other words, Applicant submits that the Rabito fails to teach that detection of GFR labels and perfusion measurement labels would require “...alternately determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers...” which is recited in claim 28.

IV. Rabito also fails to teach “... separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and, alternately with respect thereto...separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector” (Emphasis added).

On page 2 of the Advisory Action of December 23, 2008, the Office states that “...Rabito teaches detecting fluorescence substances and detecting radioactive substances (col. 3, 53-64)”. Applicant submits the Office has mixed and matched terms, phrases and concepts found in Rabito to form a seemingly justified, but ultimately incorrect, basis for rejection of claim 28.

For example, while Rabito mentions the concepts of detection of fluorescent substances, the detection of radioactive substances, as well as the terms “radiodetector” and “photodetector”, Rabito nowhere provides a single instance of all of these together as part of a single method. Contrary to the Office’s misinterpretation of Rabito, the reference, at col. 3 lines 55-58, explicitly states the following: “In some preferred embodiments the detectable substance is radioactive, and the detector includes a radiodetector; OR, the detectable substance is fluorescent, and the detector includes a photodetector...” (emphasis added).

Applicant submits that it is apparent in col. 3, lines 55-58, that Rabito seeks to include only one type of detector for measuring one type of substance that emits one type of energy.

V. Rabito fails to disclose: “wherein the at least one first detector and the at least one second detector are fixedly arranged in a specific spatial arrangement relative to each other”

As described in sections I-IV above, Applicant submits that Rabito does not even disclose “...detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector...” **and** “...separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.” Thus Applicant submits that Rabito also fails to disclose “wherein the at least one first detector and the at least one second detector are fixedly arranged in a specific spatial arrangement relative to each other” as required by claims 22 and 28.

Rejection Under 35 U.S.C. § 102

On page 3 of the Office Action, the PTO has rejected claims 22 and 28 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent 5,301,673 to Rabito *et al.* (hereafter “Rabito”). Applicant traverses this rejection for the reason set forth below.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). See generally MPEP § 2131.

Applicant submits that several differences between Rabito and the claimed invention have already been discussed above, as well as in a previous response. With respect to claim 22, Rabito fails to disclose, “...simultaneously determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers at identical projection angles, wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by

at least one second detector, wherein the at least one first detector and the at least one second detector are fixedly arranged in a specific spatial arrangement relative to each other.”

Additionally, with respect to claim 28, Rabito fails to disclose “alternately determining in vivo distributions of bioluminescent and/or fluorescent markers and in vivo distributions of radioactive markers with a common measurement apparatus at identical projection angles, wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and, alternately with respect thereto, the distribution of the radioactive markers is determined by separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, wherein the at least one first detector and the at least one second detector are fixedly arranged in a specific spatial arrangement relative to each other.”

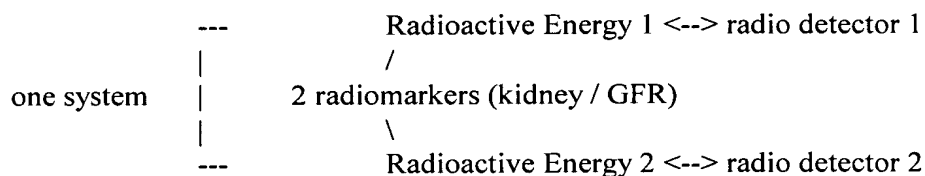
For example, Rabito states that:

[a] substance, or a plurality of substances, can be detectable by different radiation energies; for example, two or more filtration markers can be radiolabelled using labels having two different emission energies; and two or more parameters of a single organ, or the function of two or more organs, can be simultaneously monitored. For example, one labelled substance can be one that is effective for determining GFR, and the other can be one that is effective in determining kidney perfusion rate; simultaneously monitoring these two markers, using different labels so they can be distinguished, provides information about the kidney function at the nephron level.

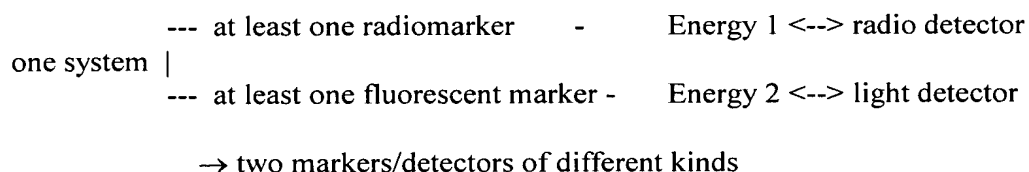
(Emphasis added). See Rabito at col. 15 lines 44-56. Rabito also states that “the detectable substance...need not be a radioactive substance, detectable by a radiodetector...[i]t can be a fluorescent substance, for example detectable by a photodetector.” See Rabito at col. 14, lines 51-60.

Applicants submit that the “two or more filtration markers” discussed above, while possibly “having two different emission energies” are actually stated in Rabito in the context of being “radiolabelled”, *i.e.*, all of these markers are of one and the same kind: radio-markers. Thus, in Rabito, “different emission energies” means different emission energies of

the kind only emitted by radiolabels, *i.e.*, radioactive energy. This particular embodiment of Rabito relied on by the Office could at best be depicted, with all markers being radioactive and all detectors suited for detecting radioactivity as follows:



In contrast to Rabito, claims 21 and 28 provide for: “...detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector...” **and** “...separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector.” An exemplary (and non-limiting) embodiment of the presently claimed invention could be depicted as follows:



Thus, Applicant submits that Rabito does not actually disclose “...separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector...” **and** “...simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector” as recited in claim 21, nor does Rabito actually disclose “...separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector **and**, alternately with respect thereto...separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector” (emphasis added) as recited in claim 28.

Additionally, with respect to the Office's arguments that Rabito discloses detecting fluorescence substances and detecting radioactive substances, Applicant respectfully disagrees. Col. 3, lines 53-58 of Rabito are reproduced as follows:

In preferred embodiments the detector specifically responds to radiant energy from the detectable substance. In some preferred embodiments the detectable substance is radioactive, and the detector includes a radiodetector; or, the detectable substance is fluorescent, and the detector includes a photodetector. The radiodetector can be a scintillator such as, for example, a NaI, CaF, CaI, or BaF detector; or the detector can be a non-scintillating detector such as, for example, a CdTe detector, or any solid, gas, or liquid type radiodetector as appropriate for the particular radiation to be detected.

(Emphasis added).

Applicant recognizes that Rabito describes separate embodiments that include detecting either fluorescent markers or radioactive markers. For example, Rabito could be depicted as:

first system	---	radio markers -	Energy 1 <--> Radiodetector

		OR	
second system	---	fluorescence markers -	Energy 2 <--> Lightdetector

Thus, due to the distinct physical effects utilized by the distinct detectors, a system of the first kind (*e.g.* radioactive) is not compatible with the system of the second kind (*e.g.* fluorescent).

In contrast, an exemplary (and non-limiting) embodiment of the presently claimed invention could be depicted as follows:

one system --- at least one radiomarker - Energy 1 <--> Radiodetector
 |
 --- at least one luminescent marker - Energy 2 <--> Lightdetector
 → two markers/detectors of different kinds.

Thus, as stated in a previous response and subsequently acknowledged by the office, and as reiterated here, Applicant submits that Rabito provides detecting fluorescent markers or detecting radioactive markers, not a method that detects both fluorescent markers and radioactive markers as required by independent claims 22 and 28.

For at least the reasons discussed above, Rabito does not anticipate claims 22 and 28 because Rabito fails to disclose all the features of claims 22 and 28. Reconsideration and withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

On pages 4-6 of the Office Action of May 13, 2008, the PTO has rejected claim 25 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rabito in view of U.S. Patent 6,232,107 to Bryan *et al.* (hereafter “Bryan”); claim 26 as allegedly being unpatentable over Rabito in view of U.S. Patent Application 2003/0101466 to Turner (hereafter “Turner”); claim 27 as allegedly being unpatentable over Rabito, in view of Turner, further in view of U.S. Patent 6,312,961 to Voirin *et al.* (hereafter “Voirin”); claims 23, 24, 29-34, and 36-41 as allegedly being unpatentable over Rabito in view of Turner, in view of Voirin, further in view of U.S. Patent 5,678,550 to Bassen *et al.* (hereafter “Bassen”); and claim 35 as allegedly being unpatentable over Rabito, in view of Turner, in view of Voirin, in view of Bassen, and further in view of U.S. Patent Application 2002/0042566 to Matsuzaki *et al.* (hereafter “Matsuzaki.”) Applicant traverses these rejections for the reasons set forth below.

The framework for the objective analysis for determining obviousness under §103 requires:

1. Determining the scope and content of the prior art;
2. Ascertaining the differences between the claimed invention and the prior art;
3. Resolving the level of ordinary skill in the pertinent art; and
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Teleflex, Inc. v. KSR Int'l Co., 127 S. Ct. 1727, 82 USPQ2d 1385 (2007); *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

As outlined above, with respect to the rejections of independent claims 22 and 28, Rabito fails to disclose, teach, or suggest each of the features of either claim 22 or claim 28. With respect to the dependent claims rejected under §103, the PTO has attempted to combine Rabito in various combinations with Bryan, Turner, Voirin, Bassen, and Matsuzaki. None of these references, taken either individually or in combination with Rabito, cures the fundamental deficiencies in Rabito outlined above.

Claims 23-26, 33, 35, 39 and 41

Applicant respectfully traverses the 103 rejections of claims 23-26. Applicant submits that Rabito does not teach or suggest, among other things, “simultaneously determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers at identical projection angles, wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, wherein the at least one first detector and the at least one second detector are fixedly arranged in a specific spatial arrangement relative to each other” (emphasis added), as recited in independent claims 22, from which claims 23-26 ultimately depend. None of the of Bryan, Turner, Voirin, and Bassen, taken either individually or in combination with Rabito, cures these fundamental deficiencies of Rabito.

For example, Bryan, Turner, Voirin, and Bassen fail to teach or suggest the “simultaneously determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers at identical projection angles, wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, wherein the at

least one first detector and the at least one second detector are fixedly arranged in a specific spatial arrangement relative to each other” (emphasis added). In contrast to the presently claimed method, the cited documents do not show all of: (1) a first detector and a second detectors (2) the “...detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector...” and “...simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector”, or (3) “simultaneously determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers at identical projection angles” (emphasis added) as recited in claim 22.

Since, none of these additional references does anything to resolve the fundamental deficiencies in Rabito, Applicant submits that no combination of these references can properly render independent claim 22 obvious and that these dependent claims are non-obvious for at least the same reasons as their respective independent claims.

Claims 27 and 29-41

Applicant respectfully traverses the 103 rejections of claims 27 and 29-41. Applicant submits that Rabito does not teach or suggest, among other things, “simultaneously determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers at identical projection angles, wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, wherein the at least one first detector and the at least one second detector are fixedly arranged in a specific spatial arrangement relative to each other” (emphasis added), as recited in independent claims 22, from which claims 27 and 29-41 each ultimately depend. None of the cited documents of Bryan, Turner, Voirin, and Bassen, and Matsuzuki taken either individually or in combination with Rabito, cures these fundamental deficiencies of Rabito.

For example, Bryan, Turner, Voirin, Bassen and Matsuzuki fail to teach or suggest the simultaneous “simultaneously determining in vivo distributions of bioluminescent and/or

fluorescent markers and radioactive markers at identical projection angles, wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, wherein the at least one first detector and the at least one second detector are fixedly arranged in a specific spatial arrangement relative to each other.” In contrast to the presently claimed method, the cited documents do not show: (1) a first detector and a second detectors (2) the “...detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector...” and “...simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector”, or (3) “simultaneously determining in vivo distributions of bioluminescent and/or fluorescent markers and radioactive markers at identical projection angles” (emphasis added) as recited in claim 22.

Additionally, the Office’s attempts to combine these cited documents with Rabito to incorporate a CCD camera and a SPECT detector are futile, as Rabito and these reference fail to teach or suggest the “...detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector...” and “...simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector” as recited in claim 22.

Since, none of these additional references does anything to resolve the fundamental deficiencies in Rabito, Applicant submits that no combination of these references can properly render independent claim 22 obvious and that these dependent claims are non-obvious for at least the same reasons as their respective independent claims.

CONCLUSION

Applicant submits that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date 4/13/09

By P.D.S.

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5540
Facsimile: (202) 672-5399

Paul D. Strain
Attorney for Applicant
Registration No. 47,369